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RAW SEQUENCE LISTING   DATE: 07/24/2002
PATENT APPLICATION: PCT/US02/21090   TIME: 11:49:19

Input Set : **A:\Sequence**
Output Set: **N:\CRF3\07242002\PU21090.raw**

#11/K.T.
8/20
Raw
Seq.
Listing

```
     3 <110> APPLICANT: Isis Pharmaceuticals, Inc.
     4        C. Frank Bennett
     5        Susan M. Freier
     7 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF HKR1 EXPRESSION
     9 <130> FILE REFERENCE: RTSP-0386
C--> 11 <140> CURRENT APPLICATION NUMBER: PCT/US02/21090
C--> 11 <141> CURRENT FILING DATE: 2002-07-02
    11 <150> PRIOR APPLICATION NUMBER: 09/898,556
    12 <151> PRIOR FILING DATE: 2001-07-03
    14 <160> NUMBER OF SEQ ID NOS: 89
    17 <210> SEQ ID NO: 1
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    19 <212> TYPE: DNA
    20 <213> ORGANISM: Artificial Sequence
    22 <220> FEATURE:
    24 <223> OTHER INFORMATION: Antisense Oligonucleotide
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    33 <213> ORGANISM: Artificial Sequence
    35 <220> FEATURE:
    37 <223> OTHER INFORMATION: Antisense Oligonucleotide
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    44 <211> LENGTH: 2772
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    46 <213> ORGANISM: Homo sapiens
    48 <220> FEATURE:
    50 <221> NAME/KEY: CDS
    51 <222> LOCATION: (3)...(2096)
    53 <400> SEQUENCE: 3
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    55        Gly Ala Leu Ser Trp Leu Gly Pro Gly Lys Ala Ser Leu Leu Arg
    56         1               5                  10                  15
    58     tct ttc cca cac ctc tgc tcc ttg tta cct gac ttt cgg ctt cag gat    95
    59     Ser Phe Pro His Leu Cys Ser Leu Leu Pro Asp Phe Arg Leu Gln Asp
    60                    20                  25                  30
    62     ccg cgg cgt gca ccc gcg ttc cat ctg tct tct gag act ttg ccc ttc   143
    63     Pro Arg Arg Ala Pro Ala Phe His Leu Ser Ser Glu Thr Leu Pro Phe
    64                    35                  40                  45
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66    tcc agg aag agc act cag gag acc agg aaa atg gct aca ggg ctc ctg    191
67    Ser Arg Lys Ser Thr Gln Glu Thr Arg Lys Met Ala Thr Gly Leu Leu
68            50                  55                  60
70    aga gcc aaa aaa gag gcg ttc gtg gca ttc agg gat gtg gct gtg tac    239
71    Arg Ala Lys Lys Glu Ala Phe Val Ala Phe Arg Asp Val Ala Val Tyr
72            65                  70                  75
74    ttc acc cag gag gag tgg agg ttg ttg agc cct gct cag agg acc ctg    287
75    Phe Thr Gln Glu Glu Trp Arg Leu Leu Ser Pro Ala Gln Arg Thr Leu
76     80                  85                  90                  95
78    cac agg gag gtg atg ctg gag act tat aac cat ctg gtc tca ctg gaa    335
79    His Arg Glu Val Met Leu Glu Thr Tyr Asn His Leu Val Ser Leu Glu
80                    100                 105                 110
82    att cca tct tct aaa cca aaa ctc att gct cag ctg gag cga ggg gaa    383
83    Ile Pro Ser Ser Lys Pro Lys Leu Ile Ala Gln Leu Glu Arg Gly Glu
84            115                 120                 125
86    gcg ccc tgg aga gag gag aga aaa tgt cca ctg gac ctc tgt cca gaa    431
87    Ala Pro Trp Arg Glu Glu Arg Lys Cys Pro Leu Asp Leu Cys Pro Glu
89            130                 135                 140
91    tcg aag cca gaa att caa ctt agt ccc tcc tgc cct ctg att ttc tcc    479
92    Ser Lys Pro Glu Ile Gln Leu Ser Pro Ser Cys Pro Leu Ile Phe Ser
93            145                 150                 155
95    agt cag caa gct ctc agc caa cat gtg tgg ctg agt cat ctc tct cag    527
96    Ser Gln Gln Ala Leu Ser Gln His Val Trp Leu Ser His Leu Ser Gln
97    160                 165                 170                 175
99    ctg ttt tca agt tta tgg gca gga aat cct ctc cac ctg gga aaa cac    575
100   Leu Phe Ser Ser Leu Trp Ala Gly Asn Pro Leu His Leu Gly Lys His
101                   180                 185                 190
103   tat cca gaa gat cag aaa caa cag cag gat cca ttc tgc ttt agt ggc    623
104   Tyr Pro Glu Asp Gln Lys Gln Gln Gln Asp Pro Phe Cys Phe Ser Gly
105                   195                 200                 205
107   aaa gca gaa tgg att caa gag gga gaa gac tcc aga ctc ctg ttt ggg    671
108   Lys Ala Glu Trp Ile Gln Glu Gly Glu Asp Ser Arg Leu Leu Phe Gly
109           210                 215                 220
111   aga gta agc aaa aat ggc act tca aag gca ctt tcc agc cca cct gaa    719
112   Arg Val Ser Lys Asn Gly Thr Ser Lys Ala Leu Ser Ser Pro Pro Glu
113           225                 230                 235
115   gaa caa cag cca gca cag tcc aag gaa gac aac aca gtg gtg gat ata    767
116   Glu Gln Gln Pro Ala Gln Ser Lys Glu Asp Asn Thr Val Val Asp Ile
117   240                 245                 250                 255
119   ggg tcc agc cct gaa cgg agg gca gat cta gag gaa aca gac aaa gta    815
120   Gly Ser Ser Pro Glu Arg Arg Ala Asp Leu Glu Glu Thr Asp Lys Val
121                   260                 265                 270
123   ttg cat ggt tta gaa gtc tca gga ttt gga gaa atc aaa tat gaa gag    863
124   Leu His Gly Leu Glu Val Ser Gly Phe Gly Glu Ile Lys Tyr Glu Glu
125                   275                 280                 285
127   ttt ggg cca ggc ttt atc aag gag tca aac ctc ctt agc ctc cag aag    911
128   Phe Gly Pro Gly Phe Ile Lys Glu Ser Asn Leu Leu Ser Leu Gln Lys
129           290                 295                 300
131   aca caa act ggg gag aca cct tac atg tac act gag tgg gga gac agc    959
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132   Thr Gln Thr Gly Glu Thr Pro Tyr Met Tyr Thr Glu Trp Gly Asp Ser
133       305                 310                 315
135   ttt ggc agt atg tca gtc ctc atc aaa aac cca agg aca cac tct ggg   1007
136   Phe Gly Ser Met Ser Val Leu Ile Lys Asn Pro Arg Thr His Ser Gly
137   320                 325                 330                 335
139   gga aag cct tat gtg tgc agg gaa tgt ggg cga ggc ttt acg tgg aag   1055
140   Gly Lys Pro Tyr Val Cys Arg Glu Cys Gly Arg Gly Phe Thr Trp Lys
141                   340                 345                 350
143   tca aac ctg atc aca cat cag agg aca cac tca ggg gag aaa cct tat   1103
144   Ser Asn Leu Ile Thr His Gln Arg Thr His Ser Gly Glu Lys Pro Tyr
145                   355                 360                 365
147   gtg tgc aag gat tgt gga cga ggc ttt act tgg aag tcg aac ctc ttt   1151
148   Val Cys Lys Asp Cys Gly Arg Gly Phe Thr Trp Lys Ser Asn Leu Phe
149       370                 375                 380
151   aca cat cag cgg aca cac tca ggg ctc aag cct tat gtg tgc aag gaa   1199
152   Thr His Gln Arg Thr His Ser Gly Leu Lys Pro Tyr Val Cys Lys Glu
153       385                 390                 395
155   tgt ggg cag agc ttt agc ctg aag tca aac ctc att acc cac cag agg   1247
156   Cys Gly Gln Ser Phe Ser Leu Lys Ser Asn Leu Ile Thr His Gln Arg
157   400                 405                 410                 415
159   gcg cac act ggg gag aag cct tat gtt tgc agg gaa tgt ggg cgt ggc   1295
160   Ala His Thr Gly Glu Lys Pro Tyr Val Cys Arg Glu Cys Gly Arg Gly
161                   420                 425                 430
163   ttt cgc cag cat tca cac ctg gtc aga cac aag agg aca cat tca gga   1343
164   Phe Arg Gln His Ser His Leu Val Arg His Lys Arg Thr His Ser Gly
165           435                 440                 445
167   gag aag cct tac att tgc agg gag tgt gag caa ggc ttt agc cag aag   1391
168   Glu Lys Pro Tyr Ile Cys Arg Glu Cys Glu Gln Gly Phe Ser Gln Lys
169           450                 455                 460
171   tca cac ctc atc aga cac tta agg aca cac aca gga gag aag cct tat   1439
172   Ser His Leu Ile Arg His Leu Arg Thr His Thr Gly Glu Lys Pro Tyr
173       465                 470                 475
175   gta tgc aca gaa tgt ggg cgt cac ttt agc tgg aaa tca aac ctc aaa   1487
176   Val Cys Thr Glu Cys Gly Arg His Phe Ser Trp Lys Ser Asn Leu Lys
177   480                 485                 490                 495
179   aca cac cag agg aca cac tca ggg gtt aaa cct tat gtc tgc ctg gag   1535
180   Thr His Gln Arg Thr His Ser Gly Val Lys Pro Tyr Val Cys Leu Glu
181                   500                 505                 510
183   tgc ggg cag tgc ttt agc ctg aag tca aac ctt aac aaa cac cag agg   1583
184   Cys Gly Gln Cys Phe Ser Leu Lys Ser Asn Leu Asn Lys His Gln Arg
185                   515                 520                 525
187   tca cac acg ggg gag aag cca ttt gta tgt acg gag tgt ggg cga ggc   1631
188   Ser His Thr Gly Glu Lys Pro Phe Val Cys Thr Glu Cys Gly Arg Gly
189           530                 535                 540
191   ttt acc cgg aaa tca acc ctg atc acg cac cag agg aca cac tca ggg   1679
192   Phe Thr Arg Lys Ser Thr Leu Ile Thr His Gln Arg Thr His Ser Gly
193       545                 550                 555
195   gag aag cca ttt gta tgt gct gag tgt gga cga ggc ttt aat gat aag   1727
196   Glu Lys Pro Phe Val Cys Ala Glu Cys Gly Arg Gly Phe Asn Asp Lys
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197   560                565                570                575
199   tcc acc ctc att tca cac cag agg aca cat tca ggg gaa aag cct ttt   1775
200   Ser Thr Leu Ile Ser His Gln Arg Thr His Ser Gly Glu Lys Pro Phe
201               580                585                590
203   atg tgc agg gag tgt ggc aga agg ttt cgg cag aag cct aac ctg ttt   1823
204   Met Cys Arg Glu Cys Gly Arg Arg Phe Arg Gln Lys Pro Asn Leu Phe
205               595                600                605
207   agg cac aag agg gca cac tca ggt gcc ttt gtg tgc agg gag tgt ggg   1871
208   Arg His Lys Arg Ala His Ser Gly Ala Phe Val Cys Arg Glu Cys Gly
209               610                615                620
211   caa ggc ttt tgt gct aag tta act ctc att aaa cac cag aga gca cac   1919
212   Gln Gly Phe Cys Ala Lys Leu Thr Leu Ile Lys His Gln Arg Ala His
213          625                630                635
215   gca ggg ggg aag cct cat gtg tgc agg gag tgt ggg caa ggc ttt agc   1967
216   Ala Gly Gly Lys Pro His Val Cys Arg Glu Cys Gly Gln Gly Phe Ser
217   640                645                650                655
219   cgg cag tca cac ctc att aga cac cag agg aca cat tca gga gag aag   2015
220   Arg Gln Ser His Leu Ile Arg His Gln Arg Thr His Ser Gly Glu Lys
221               660                665                670
223   cct tat att tgc aga aag tgt gga cgg ggc ttt agt cgg aag tcc aac   2063
224   Pro Tyr Ile Cys Arg Lys Cys Gly Arg Gly Phe Ser Arg Lys Ser Asn
225               675                680                685
227   ctt atc aga cat cag agg aca cac tca gga tag aaactttatg tgtataggga   2116
228   Leu Ile Arg His Gln Arg Thr His Ser Gly
229               675                680
231   atgtggtaca gcctttagcc aggagtcata cttcatcaga caccagagga cacacacagt   2176
232   gctgtggctt tttcagccat tgctagatac caaagtggag acattctgtg tgtgattatg   2236
233   catgagactg tactggtaag acttgtatct ccatccacct gaaggagaat tgctggctca   2296
234   ttttcaggag ccctgccctt cctcactgtg gatggtgggt tgtggaaacc cggtcaggta   2356
235   atgatagtgg caggaggcag tcaaatgccc aggcagatag gggtgggtac ctggtgaaac   2416
236   ccaaccttaa agctgaagac agtcccggct aaatcctcat actgaattga gaacctgtct   2476
237   tcccatttgg tgtgctttcc tccgattgat cccaaccctt cacctatttt acgtatacct   2536
238   gccctttcct aattggtttt tacactgctg tgcccacctt ttgagtggtg cctttgcata   2596
239   cttacaaatc agtcaacgtg tattccccta ttctgagccc ataaaagacc cagactcagc   2656
240   tgcagtgagg agagaaatca ccctgctgtg gaggttgggg accactccct gcatcccctc   2716
241   tccactgaga gctgttcttt tgctcaataa aattcttttc tacccatcct caccct        2772
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W--> 229

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247   <213> ORGANISM: Artificial Sequence
249   <220> FEATURE:
250   <223> OTHER INFORMATION: PCR Primer
252   <400> SEQUENCE: 4
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256   <210> SEQ ID NO: 5
257   <211> LENGTH: 19
258   <212> TYPE: DNA
259   <213> ORGANISM: Artificial Sequence
261   <220> FEATURE:
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RAW SEQUENCE LISTING   DATE: 07/24/2002
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Input Set : **A:\Sequence**
Output Set: **N:\CRF3\07242002\PU21090.raw**

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262 <223> OTHER INFORMATION: PCR Primer
264 <400> SEQUENCE: 5
265    acctgaccgg gtttccaca                                          19
268 <210> SEQ ID NO: 6
269 <211> LENGTH: 25
270 <212> TYPE: DNA
271 <213> ORGANISM: Artificial Sequence
273 <220> FEATURE:
274 <223> OTHER INFORMATION: PCR Probe
276 <400> SEQUENCE: 6
277    ctgcccttcc tcactgtgga tggtg                                   25
280 <210> SEQ ID NO: 7
281 <211> LENGTH: 19
282 <212> TYPE: DNA
283 <213> ORGANISM: Artificial Sequence
285 <220> FEATURE:
286 <223> OTHER INFORMATION: PCR Primer
288 <400> SEQUENCE: 7
289    gaaggtgaag gtcggagtc                                          19
292 <210> SEQ ID NO: 8
293 <211> LENGTH: 20
294 <212> TYPE: DNA
295 <213> ORGANISM: Artificial Sequence
297 <220> FEATURE:
298 <223> OTHER INFORMATION: PCR Primer
300 <400> SEQUENCE: 8
301    gaagatggtg atgggatttc                                         20
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305 <211> LENGTH: 20
306 <212> TYPE: DNA
307 <213> ORGANISM: Artificial Sequence
309 <220> FEATURE:
310 <223> OTHER INFORMATION: PCR Probe
312 <400> SEQUENCE: 9
313    caagcttccc gttctcagcc                                         20
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317 <211> LENGTH: 11173
318 <212> TYPE: DNA
319 <213> ORGANISM: Homo sapiens
321 <400> SEQUENCE: 10
322    aagcttcttg gctctctaag ttttattttc tattcactgt gagaagtact tggctattat   60
324    ttcaatattt ttcctgtccc ttttactctt tcctctcatt ctaggactcc caatttacct  120
326    gtatattgga ctgctggaaa tgtgtttctg aagattcata ttgtctcata agcttctgtt  180
328    catttttctt cagtcttttt tctctttttt gaggggtggg tggatatatg taatttctat  240
330    tcttttattt tcaaattcac taatctttct tctttttctg tttgctatta aacctgtcta  300
332    gtgaattttt aaatttcagt tgtttttttc tttccccctc ccctcctctc ccctcctctc  360
334    ccctcccctc ccctcccctc ccctcccctc ccctcccctc ccctcccctc ctcttgtttc  420
336    tgtgggtttt aggagtgctc tcaggcaaga aagccacaaa caaaattatt accccttct   480
338    gttgcaattt tttgagcata aactcttccc catcttctgg ctggttatgt atattttcca  540
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RAW SEQUENCE LISTING ERROR SUMMARY   DATE: 07/24/2002
PATENT APPLICATION: PCT/US02/21090   TIME: 11:49:20

Input Set : **A:\Sequence**
Output Set: **N:\CRF3\07242002\PU21090.raw**

Invalid Line Length:
The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:3; Line(s) 83,87,92

VERIFICATION SUMMARY   DATE: 07/24/2002
PATENT APPLICATION: **PCT/US02/21090**   TIME: 11:49:20

Input Set : **A:\Sequence**
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L:11 M:270 C: Current Application Number differs, Replaced Current Application No
L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:229 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3